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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:

Fischetti, et al.

Serial No. 10/083,462 Group: 1616

Filed: 02/27/2002 Examiner: Gollamudi, Sharmilla

The Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

RESPONSE TO OFFICE ACTION

Madam:

Please note that all correspondence should go to the address of the undersigned attorney, said address being:

2120 L Street, N.W.
Suite 210
Washington, D.C. 20037

Applicants request an interview with the examiner, primary examiner and Diane Dodesh (or Brian Stanton).

Applicants note that a Supplemental Information Disclosure Statement was filed on April 18, 2003, and after the first Office Action. Applicants see no statement from the Office that said Supplemental IDS & 1449 were considered and entered.

If the IDS & 1449 was not received, applicants respectfully request that the applicants be so

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informed, so evidence of the filing of the supplemental IDS & 1449 can be submitted, along with a substitute IDS. If the IDS was never formally entered, applicants request that said entry be made. Additionally, an IDS was previously filed in at the time the application was filed.

As all claims have been paid for, applicant desires that all claims 15-38 be considered and allowed. It is further requested that the prior amendments not entered after final now be entered.

The following claims are to be considered:

(Cancelled in Paper No. 13)

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15) A suppository enema for treating bacterial infections of the digestive tract, wherein said suppository enema is produced by the method of:

(i) obtaining an effective amount of at least one lytic enzyme genetically coded for by a specific bacteriophage specific for a specific bacteria that causes said bacterial infections of said digestive tract, said at least one lytic enzyme having the ability to digest a cell wall of a specific said bacteria, said bacteria being selected from the group consisting of *Listeria, Salmonella, E. coli, Campylobacter*, and combinations thereof;

ii) mixing said at least one lytic enzyme produced in step (a) with a suppository carrier for delivering said at least one enzyme to said digestive tract.

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16) The suppository enema according to claim 15, wherein said composition further comprises a buffer that maintains pH of a composition a range between about 4.0 and about 9.0.

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NE 17) The suppository enema according to claim 16, wherein the buffer maintains the pH of the composition at the range between 5.5 and 7.5.

NE 18) The suppository enema according to claim 18, wherein said buffer comprises a reducing reagent.

NE 19) The suppository enema according to claim 20, wherein said reducing reagent is dithiothreitol.

NE 20) The suppository enema according to claim 20, wherein said buffer comprises a metal chelating reagent.

NE 21) The suppository enema according to claim 22, wherein said metal chelating reagent is ethylenediaminetetracetic disodium salt.

NE 22) The suppository enema according to claim 20, wherein said buffer is a citrate-phosphate buffer.

NE 23) The suppository enema according to claim 15, further comprising a bactericidal or bacteriostatic agent as a preservative.

NE 24) The suppository enema according to claim 15, wherein said at least one lytic enzyme is lyophilized.

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NE 25) The suppository enema according claim 15, wherein said at least one lytic enzyme is present in a concentration of about 100 to about 100,000 active enzyme units per milliliter of fluid in the wet environment of the digestive tract

NE 26) The suppository enema according to claim 25, wherein said at least one lytic enzyme is present in a concentration of about 100 to about 10,000 active enzyme units per milliliter of fluid in the wet environment of the digestive tract.

D1 \ 1 27) A suppository enema for treating bacterial infections of the digestive tract, said suppository enema comprising:

a) an effective amount of at least one specific lytic enzyme genetically coded for by a bacteriophage specific for a specific bacteria selected from the group consisting of *Listeria, Salmonella, E. coli,* and *Campylobacter*; wherein said at least one said specific lytic enzyme is specific for and has the ability to digest a cell wall of one of said specific bacteria, said specific lytic enzyme being genetically coded for by the same said bacteriophage capable of infecting said specific bacteria being digested; and

b) a suppository carrier capable for delivering said at least one said specific lytic enzyme to said digestive tract.

2 28) The suppository enema according to claim 27, wherein said composition further comprises a

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buffer that maintains pH of a composition a range between about 4.0 and about 9.0.

29) The suppository enema according to claim 28, wherein the buffer maintains the pH of the composition at the range between 5.5 and 7.5.

30) The suppository enema according to claim 28, wherein said buffer comprises a reducing reagent.

31) The suppository enema according to claim 30, wherein said reducing agent is dithriothreitol.

32) The suppository enema according to claim 28, wherein said buffer is a metal chelating agent.

33) The suppository enema according to claim 31, wherein said metal chelating reagent is ethylenediaminetetracetic disodium salt.

34) The suppository enema according to claim 28, wherein said buffer is a citrate-phosphate buffer.

35) The suppository enema according to claim 27, further comprising a bactericidal or bacteriostatic agent as a preservative.

36) The suppository enema according to claim 27, wherein said at least one lytic enzyme is lyophilized.

37) The suppository enema according to claim 27, wherein said at least one lytic enzyme is present in a concentration of about 100 to about 100,000 active enzyme units per milliliter of fluid in the wet environment of the digestive tract.

38) The suppository enema according to claim 37, wherein said at least one lytic enzyme is present in a concentration of about 100 to about 10,000 active enzyme units per milliliter of fluid in the wet environment of the digestive tract.

RESPONSE

PRIOR ART

The present invention teaches a suppository enema which contains lytic enzymes which are specific for specific bacteria. Each lytic enzyme is specific for only one specific bacteria. The prior art cited by the examiner does not teach this feature.

The Office Action rejects claims 27-30 and 32-38 under 35 U.S.C. 103(a) as being unpatentable over Miyauchi (4,900,730) in view of Liu et al. (5, 374,545).

Applicants respectfully disagree. U.S. Patent No. 5,374,545 (Liu) does not teach, and is easily distinguishable from, the present invention. Indeed, the cited reference specifically states that the enzymes used in Liu lyse a broad spectrum of bacteria, and that the enzyme(s) is (are) of Liu are not specific for a specific bacterial species or even a specific genus. The abstract on the very first page

of the patent states that:

> A bacteriolytic enzyme complex is obtained from a bacterial culture of Bacillus pabuli strains, e.g. , isolates 350-2 (NRRL B-18446) and 391-1 (NRRL B-18447). **This bacteriolytic enzyme complex is useful as an antibacterial agent against both Gram-positive and Gram-negative bacteria**. The enzyme complex may be produced by cultivating the B. pabuli microorganisms in an aqueous medium containing cornsteep liquor, after which the lyric enzyme complex can be recovered from the fermentation broth.

Each enzyme of U.S. Patent No. 5,374,545 can kill a broad spectrum of bacteria. Col 1, lines 54-60 of 5,374,545 states:

> Also being filed with this application is a terminal disclaimer, as well as a cumulative IDS, which includes no new prior art. They may be used to hydrolyze the cells walls of many Gram-positive and Gram-negative microorganisms, including, for example, for example E. coli, Pseudomonas aeruginosa, Serratia marcescens, Corynebacterium liquefaciens and Micrococcus luteus (col 1, lines 54-60).

More importantly, col 3, lines 5-13 state:

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As may be expected, the enzyme complex from each of the different B. pabuli strains is either more or less effective one than the other against individual (i.e., pure culture) test microorganisms. **However, each of the lytic enzyme complexes was found to be effective to a significant degree against all of the test target microorganisms, and the test organism list included some known troublesome Gram-negative bacteria**, see the Table I hereinafter.

Table I clearly shows the broad spectrum of the lytic enzymes of Liu.

This contrasts with the present invention. The central idea or theme of the present invention is that a specific lytic enzyme genetically coded for by the bacteriophage is specific and lethal for one bacteria, and one bacteria only. The use of phage associated lytic enzymes in the present invention is for the treatment and lysing of only one bacteria. It does not adversely affect the natural flora of the organ being treated, unlike the invention of 5,374,545. This was explained by Drs. Fischetti and Loomis in the interview with the U.S. PTO, and is explained in the specification and defined by the claims.

Hence, the combination of Liu with Miyauchi does not teach or suggest the present invention.

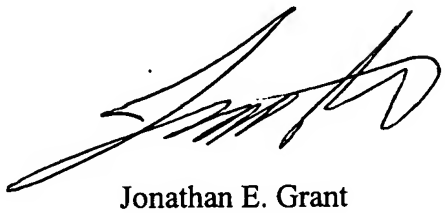
The Office Action also rejects claim 31 under 35 U.S.C. 103(a) as being unpatentable over Miyauchi in view of Liu in further view of Goldstein et al (5861295).

As this claim is dependent off of an allowable claim, the dependent claim is also allowable.

Included with this response is a cumulative IDS, which introduces no references which have not previously been cited.

The application is now in condition for allowance. Please call the undersigned at (301) 603-9071 if you have any questions or comments. Thank you.

Very truly yours,



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